BOOK REVIEWS

A Revolution in Biology and Surgery. Dead Grafts. By CHARLES NORDMANN. (From Revue des Deux Mondes, Dec. 15, 1918). Translated by M. PIETERS.

Although not the most odious of German crimes in starting the war, the most stupid is perhaps the interruption during these years of the progress of human thought, of disinterested research for the beautiful and true, the destruction of those flowers of thought which color the dark pathway of mankind.

Now a singing victory has broken down the barrier of steel and fire raised against the advance of disinterested scientific thought by the homicidal madness of a predatory race. Aside from the material losses caused by the enemy, who can estimate the immaterial ones due to the stupid furor for domination? Who can say how many Pasteurs, Claude Bernards, Henri Poincarés have been taken from humanity in the youth of their genius? Who can measure, among many other minds untouched by death, how much beauty and wisdom might have been born, had not their skill been directed toward the dark tasks of war imposed by the defence of our native soil for more than four years?

But French science is still living, and has been tonified and stimulated by victory. It is preparing to spread once more through the world with clever ideas and fruitful discoveries like those which in the past have made it famous, and enriched all who profited thereby. In this very moment when our soldiers are entering the land of the foe, so arrogant of late, (even as though to show that for France force is but the pedestal of a splendid idea), a great discovery has been made in our country. It is something which will have the largest practical applications; meanwhile, it gives us an astonishing glimpse of the very mechanism of life.

I am referring to the "dead grafts" made by two French scholars, M. Nageotte, professor of histology in the College de France, and M. Sencert, assistant professor of surgery in the Faculté de Médicine of Nancy. We must remember these two names because, as I hope to show briefly in these pages, their recent researches have introduced a new epoch in science.

We know the marvelous works of Carrel, the young Frenchman, who has found in free America, the material means to realize his original ideas. He succeeded in doing this at a time when if he had stayed in this country French scientific bureaucracy would have considered his theories scandalous and anti-administrative. He has magnified the glory of the French name by his splendid works on the culture of living tissues, on grafts, and finally, and more recently, on the treatment of war wounds. I have already had an opportunity to speak in this magazine of his very remarkable work on grafts of various organs, and particularly of vessels preserved living by various means, and notably by a process called by Carrel "cold storage." These researches are world famous and have brought the reward of the Nobel prize to their author.

It is in this field — for in science there is never an edifice so perfect that a new stone cannot be added — that Nageotte and Sencert have

been working, and we are going to see that their discovery amplifies and completes in the most unexpected manner the brilliant results obtained by Carrel. I wish to summarize the discovery in a few words before explaining the origin and methods. It is possible to graft various organs from one animal to another (and man is zoologically an animal) without these organs being preserved living. Furthermore, dead grafts seem to succeed better than living grafts; undergo in the organism where they are fixed transformations which are a veritable resurrection, reviviscence, an astonishing mechanism opening unexpected perspectives in biology.

And now — for nothing is more suggestive than the physiology of the process — I would like to show how the discovery originated.

If a synthetic view is indispensable, to know vital phenomena, or a living being, the analytic study of its elements is still more indispensable. An observer who would look down from ten kilometers above the city of Paris would certainly have a general idea of its dimensions, of its general form, of the disposition of its great thoroughfares and monuments. But, if he wants to know Paris as an active and living organism it is necessary for him to walk down its streets, to see, to hear, to mingle with its inhabitants, in order that he may observe close at hand all its intellectual and artistic treasures, all that makes the life and character of the city. So it is the same when we study a living organism; and that is why histology and the microscopic study of the elementary cells that constitute all living beings enable us to know better what are the essential, the permanent, the general, characteristic, in one word the "life phenomena" of this organism.

Before going farther — to reassure all legitimate susceptibilities — it is necessary to notice that the physical-chemical study of vital phenomena, whatever the result may be, does not free them from a mysterious character that is common to all sensible phenomena. The time is past when Haeckel could candidly believe he had solved the "riddles of the universe" in reducing all phenomena to physical and chemical notions. Even if that were possible and true, even if we could reduce all that exists in a "game" of masses, of electric energy, of chemical affinities, the door of mysteries will not have been closed, because when we go to the bottom of all things physically, we see that we do not know the essential nature of these things we call masses, electric energy, or chemical affinities.

Science never says the final word. It can attempt a classification and isolation of phenomena, but it can never prevent man from further scientific contemplation. All that science can do is to direct its course.

The histological study of living matters and the microscopical study of their anatomical elements and of their cells have been carried out very far in recent times, but perhaps a little too far in a purely morphological sense. Some experimenters in histology, in reaction against the too exclusive static tendency of this science, have wished to apply further the study of dynamic phenomena.

Among these, none are more suggestive in the formation of living tissue than the regenerative tendency which allows us to notice the restoration of flesh and destroyed organs. It is precisely out of the cicatrization of wounds that Nageotte and Sencert have made their splendid discoveries.

I apologize for these somewhat lengthy and technical remarks in introducing our main subject, but this is a question of phenomena of great interest, which although microscopic, it is necessary to under-

stand, in order to discern their great importance; for in science, contrary to what happened in fairy tales, real beauty is chiefly beautiful without a veil and wonder only arises from clearness.

The most important tissue of the human body is the connective tissue, that serves, as its name indicates, as a frame for the various elements of the body, and that constitutes the major part of what we commonly call the flesh, the bones, and the cartillage. This tissue is seen to be constituted, when examined with a microscope of very great magnifying power, of an abundant network of fibres whose diameter varies from a few thousandths of millimeters to some hundredths of millimeters. The network is cut again by a quantity of slits and composes a vast spongy system. In these webs, imbibed with a serosity that is a part of the "milieu interieur" of the human body and that is renewed without intermission we find the few scattered cells, which are the elements of the living protoplasma.

Various theories have been expressed in order to explain the formation of this intercellular network which occupies the greatest part of the connective tissues.

Some people think that this substance is formed by a kind of secretion of the cells that live in it as the compartments of the hive are made by the bees; while others think that it is formed at the expense of the substance of the cells, or rather of their exterior parts, the exoplasma. Now, in studying directly the evolution of scars with the microscope, by means of the classical methods of differentiation and coloration, M. Nageotte and Sencert have been led to the conclusion that the fundamental substance (it is so that they call it with a very appropriate term) of this connective network is formed by direct transformation of the fibrine that appears in the scar. We know that fibrine is the substance that forms in the blood and produces its coagulation when coming out the vessel. Examining a cicatrization in its various phases with the microscope we see that this plexus of fibrine which is born out of the blood plasma is transformed by imperceptible degrees till it presents the characteristics and the disposition of the fibres of the fundamental connective substance. The fibres gather progressively and constitute the connective fasciculi formed by parallel fibres. This uninterrupted metamorphosis is interesting to follow with the microscope.

The conclusion of these experiments, which has been confirmed by others, is that the intracellular substances of the connective tissue are formed directly by coagulation of the blood plasma. In consequence, and this replies to a long debated question, these substances are not more living than the plasma itself. I shall not review here the characteristics of the living substance which are irritability, the ability of reproduction, and of adaption to environment. It follows — and this is true in regard to all the conceptions, however varied, and of all the definitions of life — that the fundamental substance of the connective tissue is not living, while on the contrary the connective tissue cells are living, and this brings us immediately to the following curious conclusion to which we will return. If we consider the great volume and weight of the intracellular connective tissue in the human body we see that, for instance, when the body weighs 70 kg. it does not contain more than 4 or 5 kg. of real living substance.

Going back to my former analogy, the human body is a living thing in the same sense as a big city considered as a whole; the same as the weight and volume of the houses of the city contain but a feeble

fraction of living beings; so our body is only living in a light portion of its weight. This fraction is however by far the most important in its rank and its functions. Hence the solid intracellular substances are not living. If they offer specifically certain appearances of life, by their curious autonomy and their faculty of orientation, it is clearly the result of their reaction to their surrounding conditions, according to M. Nageotte's experiments. We know particularly that the coagulation of albuminoid substances is a very unstable phenomenon and is sensible to mechanical influences. This is easily shown in an experiment by Hardy, where one provokes artificially the coagulation of plexus fibres from a colloidal solution of the white of the egg.

Such are the audacious and suggestive conceptions towards which the most rigorous experimentation has led professor Nageotte, as a real man of science, without any preconceived idea, to follow its Ariadne's thread.

But then, if we frankly abandon any strange preconception and consider only the pure and simple facts, we see in the connective substance only the habitat of living cellular elements. It is this which led Professors Sencert and Nageotte to ask themselves whether this habitat, cleared of its occupants, can receive others. To perform this experiment, there is one means; that is, to kill all the cells in a fragment of connective tissue by dipping it in a solution which kills them and to put this fragment back in the living organism and to observe what happens; in brief, to perform a dead graft.

This is what Sencert and Nageotte have done, and now it remains for us to explain the results they have obtained, which I consider the most striking and the richest in consequences that biology and surgery have produced since a long time.

It is necessary to notice, before going farther, that we have here one of the clearest examples of what hypothesis and experimentation are able to do when they are intelligently united. In his immortal work on "Science and Hypothesis" Henri Poincaré maintained the idea, which had a particular value coming from the greatest theorist of our time, that theories have a value in science so far as they suggest experiments. In this respect, of the various biological and philosophical theories of life, without conjecturing on their real value, it is certain that the physical and chemical doctrine of living phenomena is superior to the vitalistic doctrine, because more than the latter, the former suggests experiments and practical researches. Be that as it may, in the works of Professor Nageotte and Sencert, we see how experiment and the theory reciprocally aid in achievement. Yet Newton had admirably perceived this necessary linking "omnis enim philosophiae difficultas in eo videtur ut a phenomenis investigemus vires naturae, de inde ab his virbus demonstremus phenomena reliqua." Hence the experiments stated above have led to the hypothesis that "the connective substances are inert coagulums, formed in contact with the cells of the organism and serving them as an habitat; thus we may suppose that these substances, borrowed from dead tissues and grafted in the midst of living tissues will be incorporated, without, on the one hand being eliminated like a foreign body, and on the other hand, without being destroyed by the phagocytes which annihilate living substances introduced into the organism.

It would be impossible to explain here in detail the long series of splendid experiments progressively conducted, which in the hands of M. Sencert and Nageotte has shown the foundation of their audacious hypothesis in reality. I will restrain myself — omitting all

the stages lying between, all the difficulties and fruitful gropings — to the indication of the most recent, the most demonstrative, the most delicate and the most daring of these experiments.

The two physicians have grafted, in various conditions, fragments of dead organs in the place of identical fragments taken from the same organs of a living animal.

They have laid open and resected to a length of several centimeters certain extensor tendons of the toes of dogs put to sleep with chloroform. They have replaced the absent substance by the suture of a piece of a dead tendon taken from a dog, previously killed for another purpose. These dead grafts had been preserved more than one month in alcohol. Several weeks after the operation, the dog that had rapidly recovered the integral use of its limbs, was examined microscopically. "*The operated tendons differed in no way from the corresponding tendons of the opposite paw. The dead tendons were a constituent part of the living tendons, they possessed all their morphological and physiological characteristics. Furthermore, no matter how great the magnifying power of the microscope, it was absolutely impossible to distinguish where the tendons ended, and where they started. Finally, and this is the most important discovery the graft that was dead had become perfectly alive again, its connective web had been rehabilitated with living cells that had infiltrated by degrees from the adjacent tendon.*"

In the operation performed upon dogs it is possible to see the progressive immigration, the infiltration of living cells in the empty divisions of the dead substance in its different stages. The city was dead, unpopulated but gradually the inhabitants come back and the city revives, resuscitates. Is there anything more wonderful and more fairy-like than this performance displayed in the narrow and yet gigantic field of the microscope which permits us to catch in their unveiled nakedness some of the strangest mysteries of life itself?

These dead grafts, after having been performed with organs of seccondary importance such as the tendons have been applied by the authors to those infinitely more complex and delicate organs, the arteries. They have replaced in animals fragments of carotids by fragments of dead carotids preserved in alcohol and sewn by suture on the sectioned extremities. The grafts, thanks to the technique, which requires great ability, have undergone a complete reviviscence with perfect anatomical and functional results. Still more, grafts of animals of different species have given the same results. A fragment of a sheep artery preserved in alcohol and grafted upon the carotid of a dog has been perfectly successful. It has become a dog carotid while being rehabilitated with canine cells.

Finally, in order to be definitely certain of the respective value of the dead and living grafts, the authors have performed and repeated the following experiment. They have grafted upon the same dog, on one hand, in the place of the right carotid, a dead graft which has been killed in alcohol and on the other hand in the place of its left carotid a living graft preserved by "cold storage." The result which is surprising "a priori," yet absolutely congenial with the theories of the authors, is as follows; the dead graft has been assimilated and functions much more quickly and easily than the living graft.

This evident paradox can be explained in the light of the ideas expounded above. The dead graft is a dead and uninhabited city, ready to welcome immediately the new inhabitants. On the other hand, the living graft possesses in its divisions foreign cells, the life

of which is incompatible with that of the cells of the animal, because, as Carrel has shown in his famous experiments, the living substance of an individual cannot exist in the organisms of another individual, even from an identical species, without producing toxic phenomena. It follows that the animal upon which a living graft has been fixed must first get rid of the intruded cells by means of phagocytes; only then will the animal be able to repopulate the graft with his own cells.

If I dare use the following analogy, the difference between the assimilation of the dead and the living graft is the same as that which exists between the occupation by our troops of an abandoned trench and that of a trench still occupied by the enemy.

In face of these successes, it was possible to pass without danger to the experimentation upon men, that is to say, on the surgical application of the method which from the practical point of view forms the most precious corollary of the new discovery.

It is what the two surgeons have done. After the first operation the success obtained has been wonderful. These results have been recently presented to the "Congres de Chirurgie," to the "Société de Chirurgie" and to the "Académie de Médecine." On a certain number of soldiers whose nerves had been destroyed by splinters of shell M. Nageotte and Sencert have grafted animal nerves preserved in alcohol. The results obtained have been surprising, although in some cases more than one decimeter of substance had to be replaced. The wounded soldiers have regained the absolute use of their limbs. In other wounded soldiers they have replaced in the same way the destroyed tendons by the tendons of dead animals. Perfect results. A wounded soldier had lost all the flexor tendons of the hand, regained flexion of the fingers. When the tissue of the wound was removed, one could see that three or four centimeters of each of the flexors of the fingers were lacking. Nageotte and Sencert replaced the lost substance by suture of eight grafts of dog tendons killed in alcohol. Today, this man is completely cured and moves his hand as he did before he was wounded. One could hardly over-emphasize the importance of these results in surgery.

The graft of dead parts of arteries upon animals has been brought to a successful end. There is no doubt that we will see in the near future this kind of operation performed upon man himself. This graft will have immediately a frequent application of very great importance, for instance, the cure of aneurism which has so frequently condemned a great number of individuals to death. How many lives are going to be saved by these means? Numerous are the other immediate applications of the discovery. Until now, when we had to repair an important loss of osseous substance, for instance in the case of trepanning we made the mending "in vivo" by means of bones taken from the subject himself, by "autoplastie," as they say in the "Faculte." How much easier it is going to be to make the graft by means of a veal or dog bone preserved in alcohol and of which the surgeon will have a provision in reserve in the closet of his operating room? And so for the loss of nose substance, for the "rhinoplastie," so necessary for many crippled of the war, and which a long time before the war certain diseases rendered necessary. In all these domains and in still others the way is now open, and we see all the immediate practical consequences of the suggestive works of Nageotte and Sencert.

If we look now for farther consequences in the field of probabilities the most astonishing vistas are opened before us. These perspectives

follow from what has been said and from a remarkable and unexpected biological fact that has been presented to the "Academie des Sciences" by M. Nageotte and Sencert. While observing histologically and microscopically fragments of the dead carotids grafted by them on dogs, which have been killed sometime after, they have observed and followed in all its phases the following phenomena: The arterial wall is formed as we know by several superimposed layers; the middle layer is constituted in the living artery by special cells called smooth muscular fibres separated by numerous thin and elastic "laminas." In the graft killed by alcohol, these muscular cells have disappeared and only the elastic apparatus is preserved. Now, sometime after the suture of the graft, one can see that this graft starts to be repopulated by muscular cells coming manifestly from the surrounding tissues by transversal progression and not from the extremities of the living artery by longitudinal progression. What it proves is that they are distributed at a given time in the total length of the graft, but more numerous towards the external part of the middle layer. These muscular fibres are common cells of the surrounding tissues, ordinary "fibroblastes" as we say, that transform themselves by degrees as we see with the microscope, into muscular cells with special contexture. There we see an evolution of the common cell that transforms itself into a special cell and has the characteristics of the organ into which it has infiltrated. *This fact overthrows completely current ideas on the specificity and fixity of the various kinds of cells.*

But then, the following consequences may be predicted since different organs, whatever they may be, are formed by a connective web or frame that remains when the organ is killed in alcohol and unites again in the graft with the connective frame of another organism, since on the other hand this dead grafted organ is able by its natural reaction to bring on an evolution of the ordinary cells that come alive into it, as far as to give them the specificity that characterizes them, we can imagine what follows: What would prevent us one day from grafting on an animal or a man whose kidney has to be removed, another kidney "killed" in alcohol which will revive by this "metaplastic cellular" function, at the expense of the surrounding ordinary cells and receive characteristic rhenal cells? What would prevent us from doing it with the heart, with the stomach, and with the brain? The human and social consequences would be tremendous.

What a splendid fiction work in the type of those of Vernes or Wells would it be possible to write on this topic, and is it not stimulating to think that, thanks to the wonderful and profound works of Nageotte and Sencert this fiction of today may perhaps become the reality of tomorrow.

La Psiquiatria Psicologica. By HONORIO F. DELGARDO. Lima, Samarti y Ca., 1919. 22p.

Despite all dire prophecies, psycho-analysis has been steadily extending its influence so that upon the northern half of the American continent medical doctrine, sociological and historical teaching, and even literature has felt its imprint. Now, as a review of Senor Delgardo's pamphlet, which purports to be an epitome of a larger volume on the subject, shows, South America, too, is receiving its interpretation of the new psychology. Indeed, it is claimed that the